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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Scientific Information Request on CYP2C19 Variants and Platelet Reactivity Tests

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Scientific Information Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from manufacturers of CYP2C19 variants and platelet reactivity tests. Scientific information is being solicited to inform our Comparative Effectiveness Review of Testing of CYP2C19 Variants and Platelet Reactivity for Guiding Antiplatelet Treatment, which is currently being conducted by the Evidence-based Practice Centers for the AHRQ Effective Health Care Program. Access to published and unpublished pertinent scientific information on this device will improve the quality of this comparative effectiveness review. AHRQ is requesting this scientific information and conducting this comparative effectiveness review pursuant to Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173.

DATES: Submission Deadline on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:
Online submissions: http://effectivehealthcare.AHRQ.gov/index.cfm/submit-scientific-information-packets/. Please select the study for which you are submitting information from the list of current studies and complete the form to upload your documents.

E-mail submissions: ehcsrc@ohsu.edu (please do not send zipped files - they are automatically deleted for security reasons).

Print submissions: Robin Paynter, Oregon Health and Science University, Oregon Evidence-based Practice Center, 3181 SW Sam Jackson Park Road, Mail Code: BICC, Portland, OR 97239-3098.

FOR FURTHER INFORMATION CONTACT:
Robin Paynter, Research Librarian, Telephone: 503-494-0147 or Email: ehcsrcohsu.edu.

SUPPLEMENTARY INFORMATION:
In accordance with Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, the Agency for Healthcare Research and Quality has commissioned the Effective Health Care (EHC) Program Evidence-based Practice Centers to complete a comparative effectiveness review of the evidence for testing of CYP2C19 variants and platelet reactivity for guiding antiplatelet treatment.

The EHC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by systematically requesting information (e.g., details of studies conducted) from medical device industry stakeholders through public information requests, including via the Federal Register and direct postal and/or online solicitations. We are looking for studies that report on CYP2C19 variants and platelet reactivity tests, including those that describe adverse events, as specified in the key questions detailed below. The entire research protocol, including the key questions, is also available online at:
http://effectivehealthcare.AHRQ.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=854#3962

This notice is a request for industry stakeholders to submit the following:

- A current product label, if applicable (preferably an electronic PDF file).

- Information identifying published randomized controlled trials and observational studies relevant to the clinical outcomes. Please provide both a list of citations and reprints if possible.

- Information identifying unpublished randomized controlled trials and observational studies relevant to the clinical outcomes. If possible, please provide a summary that includes the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened/eligible/enrolled/lost to withdrawn/follow-up/analyzed, and effectiveness/efficacy and safety results.

- Registered ClinicalTrials.gov studies. Please provide a list including the ClinicalTrials.gov identifier, condition, and intervention.

Your contribution is very beneficial to this program. AHRQ is not requesting and will not consider marketing material, health economics information, or information on other indications. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

In addition to your scientific information please submit an index document outlining the relevant information in each file along with a statement regarding whether or not the submission comprises all of the complete information available.

Please Note: The contents of all submissions, regardless of format, will be available to the public upon request unless prohibited by law.

The draft of this review will be posted on AHRQ's EHC program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: http://effectivehealthcare.AHRQ.gov/index.cfm/join-the-email-list1/.

The Key Questions

Key Question 1

In patient populations who are candidates for clopidogrel therapy, does genetic testing for CYP2C19 variants predict intermediate and clinical outcomes following treatment initiation?

a. What is the analytic validity (technical test performance) of the various assays used for CYP2C19 genetic testing?

b. What is the clinical validity (predictive accuracy) of genetic testing for predicting intermediate and clinical outcomes in patients who are receiving clopidogrel therapy?

c. Do the following factors modify the association between genetic test results and clinical outcomes?

i. Co-medications

ii. Patient-level factors (e.g., race or ethnicity, age, sex, disease severity, or comorbidities)

iii. Test-related factors (e.g., between-assay differences)

iv. System-level factors (e.g., settings where testing is performed)

Key Question 2

In patient populations receiving clopidogrel therapy, does phenotypic testing of platelet reactivity predict intermediate and clinical outcomes?

a. What is the analytic validity (technical test performance) of the various assays used in phenotypic testing of platelet reactivity?

b. What is the clinical validity (predictive accuracy) of phenotypic testing for predicting intermediate and clinical outcomes in patients who are receiving clopidogrel therapy?

c. Do the following factors modify the association between phenotypic test results and clinical outcomes?

i. Co-medications

ii. Patient-level factors (e.g., race or ethnicity, age, sex, disease severity, or comorbidities)

iii. Test-related factors (e.g., between-assay differences)

iv. System-level factors (e.g., settings where testing is performed)

Key Question 3

What is the comparative effectiveness of alternative test-and-treat strategies (including a no-testing strategy) for therapeutic decision making regarding antiplatelet therapy among patients who are candidates for clopidogrel-based treatment?

a. What is the comparative effectiveness of the following testing strategies on therapeutic decision making, platelet reactivity during followup, and clinical outcomes in patients who are candidates for antiplatelet treatment?

i. Genetic testing for CYP2C19

ii. Genetic testing for CYP2C19 followed by phenotypic testing for platelet reactivity

iii. Phenotypic testing for platelet reactivity

iv. No testing

b. How do modifying factors (e.g., race or ethnicity, age, sex, comorbidities, diet, or the time between conducting the test and obtaining results) affect the association of alternative phenotypic or genetic test-and-treat strategies and patient outcomes? Alternative test-guided treatments can include non-clopidogrel antiplatelet agents or high-dose clopidogrel regimens.

Key Question 4

What are the potential adverse effects or harms from genetic or phenotypic testing per se or from test-directed treatments?

Dated: DEC 2 2011

Carolyn M. Clancy, M.D.
AHRQ, Director

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